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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/540,311	12/12/2005	Meena Augustus	689290-248	4638
27162	7590	01/26/2010	EXAMINER	
CARELLA, BYRNE, CECCHI, OLSTEIN, BRODY & AGNELLO 5 BECKER FARM ROAD ROSELAND, NJ 07068				KIM, YOUNG J
ART UNIT		PAPER NUMBER		
1637				
MAIL DATE		DELIVERY MODE		
01/26/2010		PAPER		

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>	
	10/540,311	AUGUSTUS ET AL.	
	<b>Examiner</b>	<b>Art Unit</b>	
	Young J. Kim	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) Responsive to communication(s) filed on 04 September 2009.
- 2a) This action is **FINAL**.                  2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) Claim(s) 1-59 and 65-70 is/are pending in the application.
- 4a) Of the above claim(s) 1-15, 19-27 and 31-59 is/are withdrawn from consideration.
- 5) Claim(s) \_\_\_\_\_ is/are allowed.
- 6) Claim(s) 16-18, 28-30, 65 and 67-69 is/are rejected.
- 7) Claim(s) 66 and 70 is/are objected to.
- 8) Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on \_\_\_\_\_ is/are: a) accepted or b) objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) All    b) Some \* c) None of:  
 1. Certified copies of the priority documents have been received.  
 2. Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |   |   |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)  | Paper No(s)/Mail Date. _____ .                                    |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)<br>Paper No(s)/Mail Date <u>9/4/2009</u> . | 5) <input type="checkbox"/> Notice of Informal Patent Application |
|   | 6) <input type="checkbox"/> Other: _____ .                        |

## **DETAILED ACTION**

The present Office Action is responsive to the Amendment received on September 4, 2009.

### ***Election/Restrictions***

This application contains claims 1-15, 19-27, and 31-59 which are drawn to an invention nonelected without traverse in the reply filed on November 16, 2007. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

### ***Preliminary Remark***

Claims 67-70 are new.

Claims 16-18, 28-30, and 65-70 read on the elected invention and thus are prosecuted herein.

### ***Information Disclosure Statement***

The IDS received on September 4, 2009 is proper and is being considered by the Examiner.

### ***Claim Rejections - 35 USC § 112***

The rejection of claims 16-18, 28-30, 65 and 66 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter, made in the Office Action mailed on June 2, 2009 is withdrawn in view of the Amendment received on September 4, 2009.

### ***Rejection, Necessitated by Amendment***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 16-18, 65, 67, and 68 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 16 recites the phrase, “of the same organ.”

Claim 16, while reciting that the method is for identifying a cancerous cell, does not recite any previous step of determining step from an organ. Therefore, the phrase lacks a proper antecedent basis.

Claims 17, 18, 65, 67, and 68 are indefinite by way of their dependency on claim 16.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 16-18, 28-30, and 69 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of identifying a cancerous cell of the breast or a method of detecting breast cancer, does not reasonably provide enablement for a method of identifying or detecting any cancer. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Factors to be considered in determining whether a disclosure would require undue experimentation are summarized in In Re Wands (858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988)). They include (A) the quantity of experimentation necessary, (B) the amount of direction or guidance presented, (C) the presence or absence of working examples, (D) the nature of the invention, (E) the

state of the prior art, (F) the relative skill of those in the art, (G) the predictability or unpredictability of the art, and (H) the breadth of the claims.

The Nature of the Invention, Unpredictability of the art, and Enablement Issue:

The nature of the invention relates to a highly unpredictable art of cancer diagnostics based on gene expression or gene copy number. It is well known in the art that the development of cancer involves complex cascades of biochemical reaction. Thus, the enablement issue surround on whether Applicants' discovery of increased copy numbers of a particular gene for a particular type of cancer (in the present case, breast cancer), would enable a skilled artisan to practice the invention for other types of cancers without undue experimentation.

Amount of Guidance and Absence of Working Examples:

The instant specification discloses that Applicants discovered the increased mRNA expression as well as an increased copy number of the gene, "TRIP-13" in breast cancer cell line (page 3, lines 28-32)

The instant specification provides a working example wherein FISH was conducted on breast cancer samples (page 37, line 25 through page 38).

The instant specification also provides evidence that when amplification status of TRIP13 was examined on formalin-fixed tissue microarray (TMA) containing 785 breast cancer samples by FISH, BAC probe from the TRIP13 region exhibited high-level amplification (>3 fold) in 5% of the total cases (547 samples), low level amplification (2 to 3 fold) in 29% of breast cancer samples (page 39).

While the instant specification provides various working examples for breast cancer and how TRIP13 correlates thereto, the instant specification does not provide any guidance or working example when it comes to determining/detecting cancers of other origins.

As stated previously, cancer involves multi-factorial processes, involving cascades of biochemical processes. Consequently, a particular gene marker for a particular cancer does not always equate to its successful usage for determination of other types of cancers.

Such is plainly demonstrated by Knuutila et al. (American Journal of Pathology, 1998, vol. 152, no. 5, pages 1107-1123), wherein Table 1 shows that an increase copy of the gene ABL, is found in a particular types of cancer - Chronic myeloid leukemia. Similarly, the gene, HSTF1, is found to be increased in breast cancer and esophageal carcinoma, and so on.

Therefore, it is complexly unpredictable as to whether a cancer gene marker found strictly from a single type of cancer could be used for determining other types of cancers.

As set forth in *Rasmussen v. SmithKline Beecham Corp.*, 75 USPQ2d 1297, 1302 (CAFC 2005), enablement cannot be established unless one skilled in the art "would accept without question" an Applicant's statements regarding an invention, particularly in the absence of evidence regarding the effect of a claimed invention. Specifically:

"As we have explained, we have required a greater measure of proof, and for good reason. If mere plausibility were the test for enablement under section 112, applicants could obtain patent rights to "inventions" consisting of little more than respectable guesses as to the likelihood of their success. When one of the guesses later proved true, the "inventor" would be rewarded the spoils instead of the party who demonstrated that the method actually worked. That scenario is not consistent with the statutory requirement that the inventor enable an invention rather than merely proposing an unproved hypothesis."

While one may argue that one of skill in the art could have been capable of determining whether the copy number of TRIP13 was increased in other types of cancers, this does not account for the unpredictability in the art for correlating gene markers as cancer markers, as shown above. Such argument would be what the court considered as, "little more than respectable guesses as to the likelihood of ... success" which is not a proper showing of enablement.

Therefore, for the above reasons, one of skill in the art would not be capable of practicing the invention fully commensurate in scope of the claims without undue experimentation.

***Examiner's Comment***

Mr. Alan Grant had been contacted on January 15, 2009 for negotiating claim amendment to allow the application. Since then, Mr. Grant advised the examiner of record that the application had been transferred from his firm and that he no longer had the authorization for any amendment.

Consequently, the present office action is being furnished.

Instantly claimed nucleic acid of SEQ ID NO: 1 is disclosed as encoding the protein of SEQ ID NO 7.

Baak et al. (WO 02/10436 A2, issued February 7, 2002, of record) disclose a protein which is 100% identical to instant SEQ ID NO: 7, wherein the artisan disclose that this protein is over-expressed in breast cancer samples (see claim 1).

Baak et al., however, do not disclose that the number of gene copies encoding the protein is increased in breast cancer samples.

Sutherland et al. (Acta Oncologica, 1995, vol. 34, no. 5, pages 651-656) evidences that not all genes which are amplified results in increased expression of the gene products:

"Increased expression of cyclin D1 was the most common alteration in cyclin gene expression noted in these cell lines. This gene was highly expressed in MDA-MB-134, -175, -330, and -453 cells and one of two MCF-7 variants, Compared with the level of mRNA observed in the majority of the breast cancer cell lines and in two strains of normal, non-transformed breast epithelial cells ... Cyclin D1 gene amplification was detected in six cell lines but amplification was not a prerequisite for, and did not always lead to, increased cyclin D1 expression." (page 654, 2<sup>nd</sup> column, bottom paragraph).

Therefore, one of ordinary skill in the art would not have had a reasonable expectation of success at concluding that the cause of the increased protein level determined by Baak et al. was based on the increased copy number of the gene encoding that protein.

Since there was no reasonable expectation of success, there would also have been no motivation to arrive at the claimed invention based on the disclosure of Baak et al.

Applicants are advised to limit the scope of the claims to breast cancer for the allowance of the application.

***Conclusion***

No claims are allowed.

Claims 66 and 70 are objected to for being dependent on a rejected base claim.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

***Inquiries***

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Young J. Kim whose telephone number is (571) 272-0785. The Examiner is on flex-time schedule and can best be reached from 6:00 a.m. to 2:30 p.m (M-F). The Examiner can also be reached via e-mail to [Young.Kim@uspto.gov](mailto:Young.Kim@uspto.gov). However, the office cannot guarantee security through the e-mail system nor should official papers be transmitted through this route.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Gary Benzion, can be reached at (571) 272-0782.

Papers related to this application may be submitted to Art Unit 1637 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 CFR 1.6(d)). NOTE: If applicant does submit a paper by FAX, the original copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED, so as to avoid the processing of duplicate papers in the Office. All official documents must be sent to the Official Tech Center Fax number: (571) 273-8300. For Unofficial documents, faxes can be sent directly to the Examiner at (571) 273-0785. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Young J. Kim/  
Primary Examiner  
Art Unit 1637  
1/25/2010

/YJK/